

THE EXPERIMENTAL TRANSMISSION OF GOITRE FROM MAN TO ANIMALS

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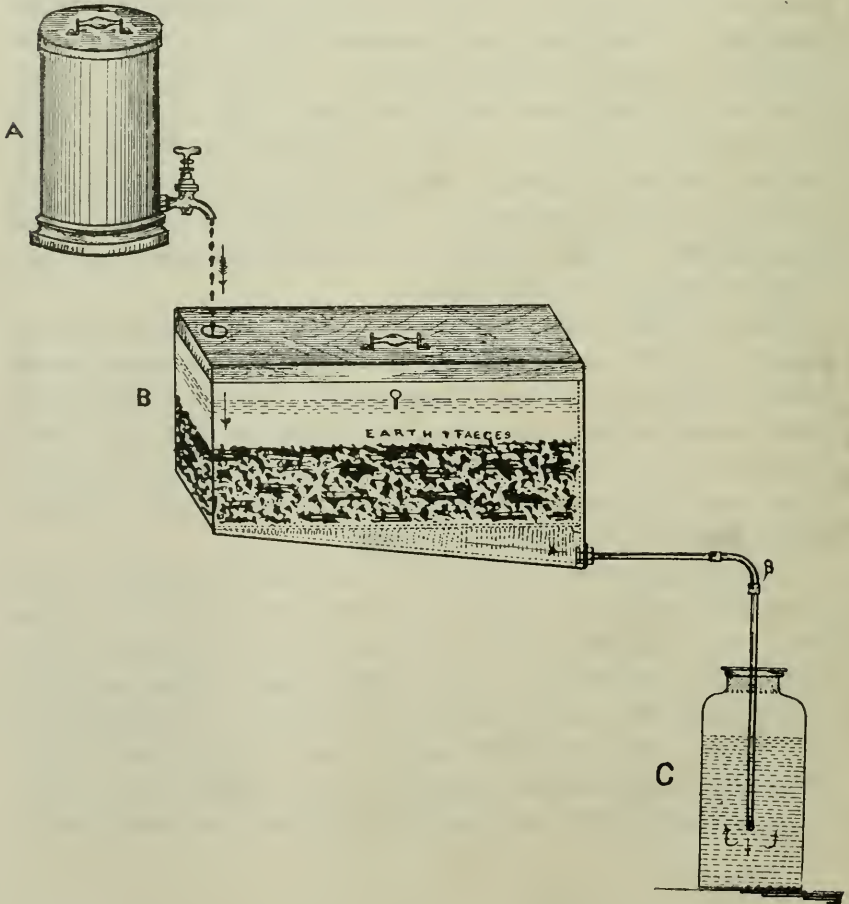
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Since the year 1906 I have repeatedly endeavoured to transmit goitre from man to animals by infecting the water supply of the latter with the faeces of sufferers from goitre. The assumption that goitre can be so conveyed follows upon the results of my former researches. I had previously employed dogs, but obtained no results of a positive character (1906-11). This was due largely to the fact that dogs suffer little from goitre in this country, though these animals are known to be frequently affected in other localities. I believe that the comparative freedom of dogs from goitre in Gilgit indicates that the infecting agent of this disease is less toxic there than elsewhere. Other facts point in the same direction, but these I hope to discuss in another place.

The possibility that an intermediate host was concerned in the spread of goitre having occurred to my mind, I suspected earthworms of playing this rôle. I, consequently, devised an experiment which would not only again test the assumption that goitre could be transmitted from man to animals by infected faeces, but would at the same time determine the influence, if any, which earthworms might possess in spreading the disease.

Female goats were selected for this dual experiment. The goats were between the ages of one and two years and were not pregnant. This latter point is of importance, as pregnancy, owing to the increased activity of the thyroid gland during that state, would vitiate the results observed on microscopical examination of this organ. The goats were brought from a non-goitrous locality, high up in the mountains, about forty miles distant from Gilgit. Their thyroid glands were carefully examined and were found to

show no signs of hypertrophy. In the majority the gland on each side could be felt only with the greatest difficulty, or could not be distinguished from the surrounding tissues. Where the organ was palpable it was found to be oval in shape and about the size of a very small almond. The goats were divided into batches, which will be referred to as: I, 'Controls' (three goats); II, 'Batch X' (six goats); III, 'Batch Y' (seven goats). Each batch was confined in a separate house, the door of which was of netted wire. The animals were all fed on the leaves and young branches of trees, in order to exclude as far as possible sources of contamination from the soil. The experiment was designed so as to foul the drinking water of 'Batches X and Y,' while that of the 'Controls' remained pure. The apparatus which I employed for this purpose is represented in the figure:—



It consisted of a covered drum, A, which was fitted with a tap; a covered wooden box, B, having a perforated false bottom of wire gauze under which was a wooden trough sloping towards an outlet pipe β . This outlet pipe led into a flask, C, which was fitted with a perforated cork so as to ensure freedom from contamination by soil, dust, etc. The drum A was filled with a non-goitre producing water which was previously boiled. A trickle of water from the drum A was allowed to pass continuously into the box B. This box was partially filled with soil taken from the most goitrous village in Gilgit. The soil was sterilized by steam at 230° F. for thirty minutes, and was then mixed with the faeces of sufferers from incipient goitre. Fresh faeces were added to the mixture several times a week during the course of the experiment. The water from the drum A trickled into the box B, saturated the mixture of sterilized earth and faeces, and, passing through the perforated bottom of the box, found its way, by means of the wooden trough and outlet pipe β , into the corked flask C. This was the only drinking water provided for the goats of 'Batches X and Y.'

A separate apparatus was used for each batch. In the case of 'Batch Y,' however, 500 earthworms were introduced into the box B. It will be seen that 'Batch X' were provided with drinking water which was grossly contaminated with the faeces of sufferers from goitre, while in the case of 'Batch Y' the drinking water contained also such additional matter as was derived from the excreta of the earthworms. The water which found its way into the stoppered bottle was in both cases foul smelling and of a dark grey colour.

The experiment was commenced on the 13th October, 1910, and terminated on the 15th December, 1910. The thyroid glands of the control goats showed no change during the sixty-four days of the experiment. In the case of the goats of 'Batches X and Y,' however, it was observed that

- (1) the animals lost in weight, due doubtless to confinement in a small hut for sixty-four days;
- (2) many of them suffered from diarrhoea;
- (3) 50 per cent. of the goats in each batch showed enlargements of the thyroid gland, which was most marked in the right side.

To facilitate examination of the necks of these animals the hair was kept closely clipped, but as measurement and photography cannot be employed in the case of animals as aids to diagnosis, palpation alone had to be relied upon during the course of the experiment. It was observed that the thyroid gland in two goats in 'Batch X' showed signs of enlargement as early as the thirteenth day of the experiment. In all cases in which enlargement occurred, a noticeable feature was the manner in which the size of the gland fluctuated. At one examination it would be found that the organ was little, if anything, larger than in the case of the controls, while a day or two later it would appear to be not less than twice the size. Goitre in man, whether artificially produced or naturally acquired, shows the same tendency to fluctuate in size in its early stages (1909) (1911, Febr.). The animals were killed on the 15th December by a Goorkha, skilled in severing the head from the body at one stroke of his kookrie (knife). The neck was dissected immediately and the gland rapidly exposed. It was observed in several cases that the size of the organ diminished considerably before it could be removed from the body. The right and left lobes of the thyroid, with their long and narrow isthmus, were rapidly dissected out and weighed. The following table shows the results in the case of the sixteen animals employed in the experiment:—

I.—'Controls,' 3 in number, which consumed only pure water:—

Weight of goat			Weight of thyroid	Proportionate weight of thyroid to body weight
1	...	60 lbs.	3.2 gms.	$\frac{1}{10,000}$
2	...	43 "	2.05 "	$\frac{1}{10,439}$
3	...	65 "	3.2 "	$\frac{1}{10,100}$

II.—'Batch X,' 6 in number, which consumed only faecally contaminated water :—

Weight of goat			Weight of thyroid	Proportionate weight of thyroid to body weight
1	...	48½ lbs.	3.6 gms.	$\frac{1}{6,654}$
2	...	26½ "	2.93 "	$\frac{1}{4,500}$
3	...	38 "	2.3 "	$\frac{1}{8,000}$
4	...	30 "	1.5 "	$\frac{1}{10,000}$
5	...	22½ "	2.32 "	$\frac{1}{4,800}$
6	...	29 "	1.35 "	$\frac{1}{10,700}$

III.—'Batch Y,' 7 in number, which consumed faecally contaminated water, as in the case of 'Batch X,' together with the excrementitious products of earthworms :—

Weight of goat			Weight of thyroid	Proportionate weight of thyroid to body weight
1	...	50½ lbs.	4 gms.	$\frac{1}{7,000}$
2	...	41½ "	4.3 "	$\frac{1}{4,850}$
3	...	56 "	3.7 "	$\frac{1}{7,530}$
4	...	55½ "	3.6 "	$\frac{1}{7,700}$
5	...	49½ "	5.4 "	$\frac{1}{4,272}$
6	...	45 "	1.9 "	$\frac{1}{11,700}$
7	...	39 "	1.9 "	$\frac{1}{10,000}$

It will be seen from the tables that the weight of the control animals' thyroid was in all cases about $\frac{1}{10,000}$ th part of the body weight. In 'Batch X' the thyroids of Nos. 4 and 6 showed no deviation from the normal weight. In two, Nos. 1 and 3, the

weight of the thyroid was considerably more than normal, while in the remaining two, Nos. 2 and 5, it was twice as much as that of the controls. In 'Batch Y' Nos. 6 and 7 had thyroid glands of the normal weight; in Nos. 1, 3 and 4 the weight of these organs was considerably more than normal; while in Nos. 2 and 5 the thyroids were more than twice the weight of those of the control animals. Allowing for variations in size of the normal thyroid of from $\frac{1}{8,000}$ th to $\frac{1}{11,000}$ th part of the body weight, it will be admitted that about 50 per cent. of the animals in 'Batches X and Y' showed enlargements of the thyroid gland.

MICROSCOPICAL APPEARANCES OF THE GLANDS

Striking differences were observed in the microscopical appearances of the thyroids in these animals. In the control animals the vesicles were found to be small, round, compact, and lined with cubical epithelium. The space between the vesicles was filled with masses of round cells, and many vesicles were seen in the field of the microscope. In the thyroids of those animals which showed the greatest increase in size as determined by weight, the vesicles were much larger, their walls markedly thinner, and their outline much more irregular, while fewer appeared in the field of the microscope than in the case of the normal gland. The epithelium lining the vesicles was much flattened, and the intervesicular cellular tissue was markedly less in amount than in the case of the normal gland. Sections of the enlarged organs often showed fields in which the colloid had fallen out during the process of staining; these fields, when viewed as a whole, had a peculiar 'netted-wire' appearance, which differed very markedly from the compact structure of the normal gland. Glands which showed an intermediate degree of enlargement presented in some parts of the section the appearances of normal tissue, while in others the dilated vesicles, flattened epithelial lining and the scarcity of intervesicular cellular tissue were characteristic of the more enlarged organs. In short, every degree of variation was met with from the small, round, compact vesicle of the normal organ to the cyst-like dilatation of the vesicle of the hypertrophied gland. In none of the enlarged organs was there any evidence of active cell proliferation or of inflammatory change. There appeared to be little or no alteration in the connective tissue stroma of the enlarged glands.

The increase in size of the hypertrophied organs was due wholly to the distension of the vesicles with colloid material. It seems evident that this distension must result in thinning and rupture of the walls of the vesicles and in the formation of small, cystic cavities in the gland; and that distension of existing vesicles, and the formation of new vesicles from the intervesicular cell masses, are the earlier stages in the development of parenchymatous goitre. In some cases colloid was seen in the vessels of the gland (Photomicrograph VI).

This experiment proves that a hypertrophy of the thyroid gland of goats can be induced by infecting the water supply with the faeces of sufferers from goitre. It is, at present, impossible to state whether this hypertrophy is due to the action of the infecting agent of goitre, or only to the organic impurity of the water thus contaminated.

Earthworms do not appear to be concerned in the spread of goitre.

Goitre is essentially a disease of country localities, that is, of localities of unprotected water supplies. In this country I have found, from a study of the topography of a very large number of villages, that the freedom, or the reverse, of any particular village from this disease depends very largely on the extent to which the drinking water is contaminated by irrigating fields, which are fertilized with human and animal excreta. The source of the water supply and the geological formations from which it is derived are, in comparison, of minor importance.

Further experiments on goats are at present in progress, with a view to confirming the results detailed above. These experiments have not long been in progress, but already five out of twelve goats which are drinking faecally contaminated water show signs of enlargement of the thyroid gland, while no changes have occurred in the thyroids of twelve control animals. The final results of these experiments and the microscopical appearances of the glands will be detailed in a subsequent report.

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DESCRIPTION OF PLATES

PLATE VIII

Fig. 1.—Photomicrograph of normal thyroid gland of goat. $\times 100$. Shows numerous rounded vesicles holding colloid. The cubical epithelial lining and the cell masses between the vesicles cannot be seen with this magnification. Section taken from the thyroid gland of control goat No. 2.

Fig. 2.—Photomicrograph of artificially produced parenchymatous goitre in goat. $\times 100$. Shows the marked dilatation of the vesicles and the thinning of their walls. Section taken from thyroid gland of goat No. 1, 'Batch Y.'

194'

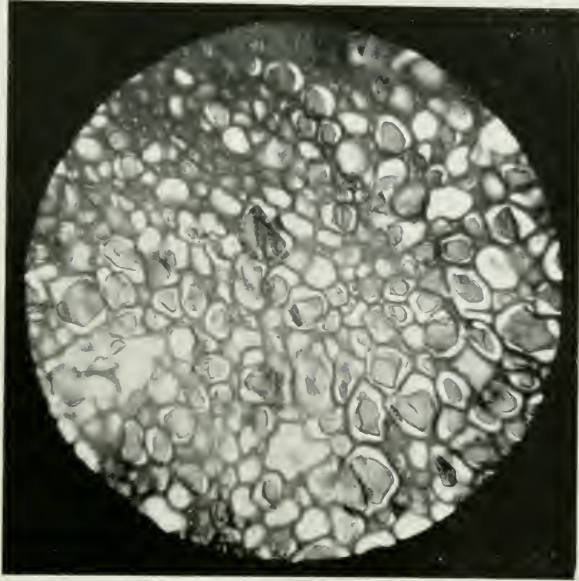


FIG. I

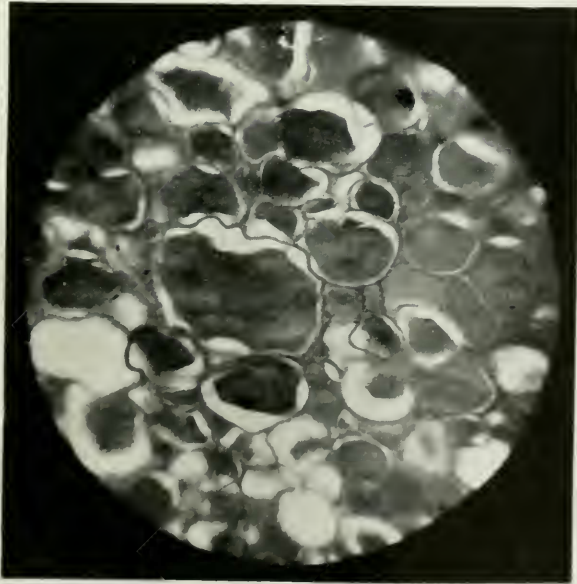


FIG. II

PLATE IX

Fig. 3.—Photomicrograph of normal thyroid gland of goat. $\times 100$. Shows same appearances as in Photomicrograph No. 1. Section taken from thyroid gland of goat No. 6, 'Batch X.'

Fig. 4.—Photomicrograph of artificially produced parenchymatous goitre in goat. $\times 100$. Shows marked dilatation of the vesicles, thinning of the vesicle walls, and the 'netted-wire' appearance alluded to in the text. Section taken from thyroid gland of goat No. 5, 'Batch Y.'

196'

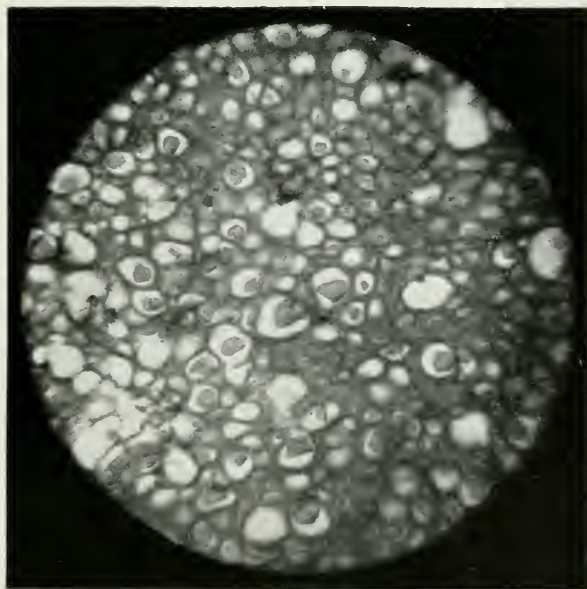


FIG. III

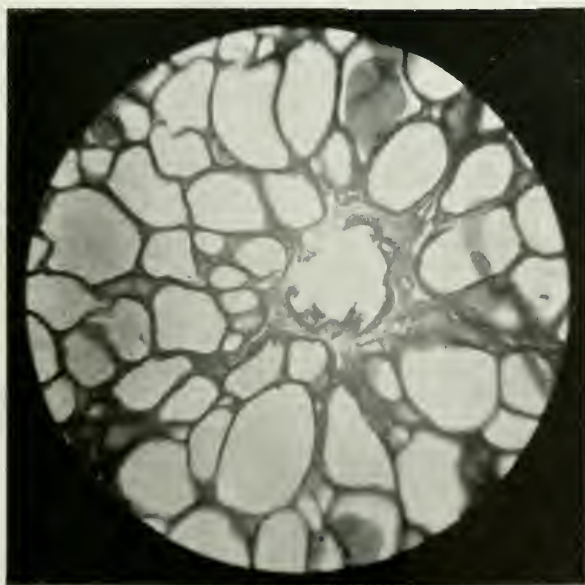


FIG. IV

PLATE X

Fig. 5.—Photomicrograph of normal thyroid gland of goat. $\times 100$. The cubical epithelial lining can be seen in a few of the vesicles. Figs. 1, 3 and 5 illustrate the variations in the size of the vesicles which are met with in the normal thyroid gland of the goat. Section taken from thyroid gland of control goat No. 5.

Fig. 6.—Photomicrograph of artificially produced parenchymatous goitre in goat. $\times 100$. Shows colloid in vessel of gland. Part of the field shows comparatively normal appearances. Photograph was taken from the same section as Fig 2.

The sections, from which the photomicrographs were taken, were stained in aqueous solutions of magenta red, picric acid and indigo carmine (Borrel's stain).

198'

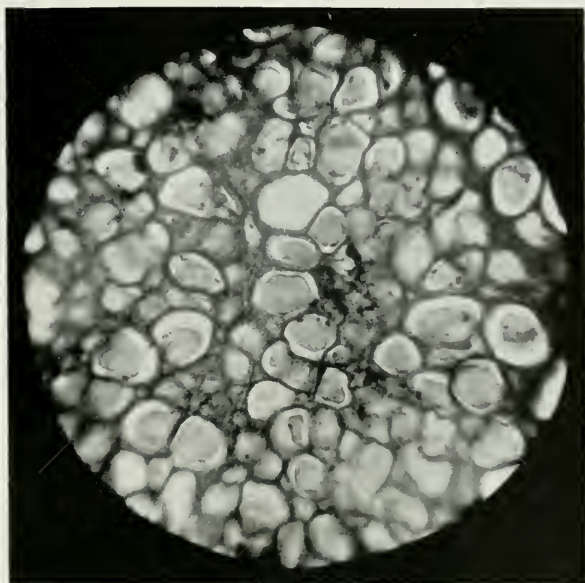


FIG. V

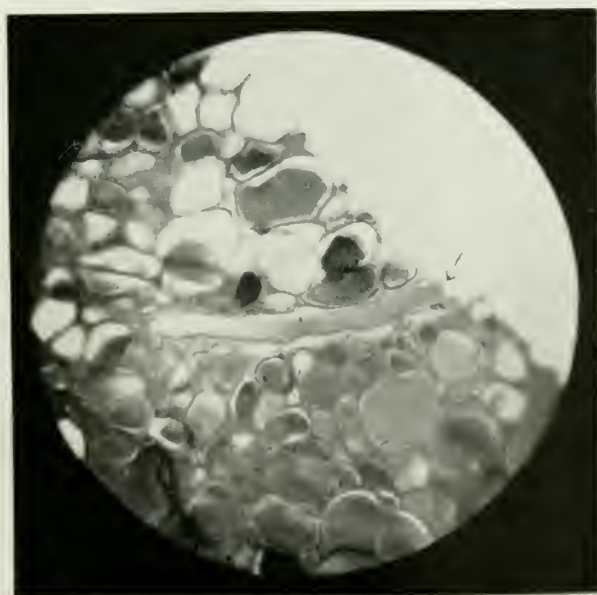


FIG. VI